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C. Davis, M. Epton, M. Frank, A. Gryshuk, N. Kenyon

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Emerging topics and new developments in the field: the 2012 International Breath Analysis Meeting.

Cristina E. Davis[1,*], Michael Epton[2], Matthias Frank[3], Amy Gryshuk[3], Nicholas J. Kenyon[4].

[1]Department of Mechanical and Aerospace Engineering, University of California, Davis, CA 95616, USA.

[2]Canterbury Respiratory Research Group, Christchurch Hospital, Christchurch, Canterbury 8022, New Zealand.

[3]Physical and Life Sciences Directorate, 7000 East Avenue, Lawrence Livermore National Laboratory, Livermore, CA 94550, USA.

[4]Division of Pulmonary, Critical Care, and Sleep Medicine, Center for Comparative Respiratory Biology and Medicine, University of California, Davis, CA 95616, USA.

[*] Correspondence: cedavis@ucdavis.edu, TEL +1.530.754.9004

Abstract. The 2012 International Breath Analysis meeting was held in Sonoma, CA (USA) from 28 OCT – 01 NOV 2012. The focus of the meeting covered several important topics within the research area, including both engineering and the biomedical sciences. As human breath analysis further develops as a multi-disciplinary field, it is clear that sensor development, instrumentation systems and algorithms play critical roles. Although much emphasis in the last decade has focused on breath biomarker compound identification and physiological relevance, we increasingly turn our attention towards portable, fieldable sensor platforms for non-invasive breath monitoring. The mission of this workshop was to assemble a group of leading experts to discuss their own research, debate trends and future directions of the field, and contemplate areas of research that deserve special attention moving forward.

Keywords: breath analysis, biomarkers, non-invasive diagnostics, exhaled breath condensate, volatile organic compounds (VOCs), sensors, mass spectrometry.

1. Introduction

The 2012 International Breath Analysis meeting was held in Sonoma, CA (USA) and was titled ***"Breath Analysis for Biomedicine and National Security: Sensor Design Issues and Strategies for Biomarker Discovery."*** The goal for the meeting was to provide an opportunity for researchers from academics, basic sciences, medicine, industrial companies and the national laboratories to meet and discuss important topics associated with breath sensor instrumentation and breath biomarker discovery. Participants were encouraged to explore potential future collaborations, and consider teaming for competitive grant proposal submissions to federal funding agencies. Interactions with industry also were expected to shed light on near-term research trends that can yield first generations of breath analysis sensor platforms.

The meeting was co-organized and co-chaired by Cristina Davis, Michael Epton, Nicholas Kenyon, Matthias Frank and Amy Gryshuk. The scientific organizing committee consisted of Raed Dweik, Wolfram Miekisch, Jane Hill, Mona Syhre, Malina Storer, and Steve Chambers. The structure of the meeting was single-track scientific sessions, with significant time for individual and group discussions. There were also two poster sessions, and two industry sessions with platform talks providing commercialization updates and future trends in the field.

The conference attracted a mix of junior and senior researchers from all sectors of breath research in engineering, medicine and chemistry. Attendees traveled from 18 countries representing 65 cities from around the world. Of a total of 125 attendees 65 were from academic institutions, 37 from industry (both large and small companies), and 20 from government agencies. The companies ranged from startup technology companies to major corporations active in the breath research field. The dynamic of the group generated discussions that were lively and beneficial to all.

There were twelve keynote speakers over the course of the meeting. The opening night keynote by Terence Risby was titled ***"Breath Analysis: Past, Present and Future. A Personal Perspective."*** It was a frank and honest assessment of where the field has traveled over the last four decades, since Pauling's first report of breath volatiles in 1971. Risby acknowledged the many opportunities of breath monitoring for health and forensic applications, while also noting the risks associated with adequate sampling methods and the role of exogenous chemicals in breath as potential obscuring factors for clinical diagnostics.

2. Scientific Tracks and Major Reports

2.1 Breath Biomarkers of Infections, Diseases and Disorders

Presentations and discussions on breath biomarkers took up several sessions of this conference, including a session on tuberculosis makers on day 1, a session on lung cancer and other malignancies on day 4, a session on infection and metabolism also on day 4 and a session on VOCs from stool and urine for disease diagnostics on day 5.

The presentations on biomarkers on day 1 were introduced by Jochen Schubert (university of Rostock, Germany) with the second plenary keynote address entitled ***"Biomarkers and Non-Invasive Biomedical Analysis – Sisyphean Task or Question of Effort?"*** He discussed a range of potential biomarker candidates that are being explored and cautioned about over-interpreting the significance of correlations between biomarkers and corresponding diseases. Correlations found may be accidental ("voodoo correlations") if the number of parameters is large and the number of measurements small. False positives and false negatives can cause problems, in particular, when disease prevalence is low and a large number of people are screened. These themes were reiterated throughout presentations and discussions during the conference.

Michael Philips (Menssana Research Inc., USA) kicked off the tuberculosis biomarker session with a keynote presentation on promising results in this area obtained over the last decade and the BreathLink point-of-care system that can deliver results in less than 10 minutes. He also discussed his current studies on investigating the possibility of identifying drug-resistant tuberculosis with a breath test. Amy Scott-Thomas (University of Otago, New Zealand) reported on a number of specific VOCs (including methyl phenylacetate, methyl nicotinate, methyl p-anisate and o-phenylanisole) that have been detected in the breath of tuberculosis patients and on investigating the optimal sampling strategy to detect those makers. Niaz Banaei (Stanford University, USA) described the ongoing efforts at Stanford to compare the diagnosis of pulmonary tuberculosis via VOC markers in breath with more established methods such as nucleic acid amplification tests and presented results on the detection of tuberculosis-specific VOCs in

breath with a novel calorimetric sensor array. Swomitra Mohanty (University of Utah, USA) described a VOC biomarker sensor based on TiO2 nanotubes and presented promising results on detecting some of the abovementioned markers in the presence of interferents (other organics, humidity) with the sensor.

Breath biomarkers in "lung cancer and other malignancies" and in "infection and metabolism" were the subject of two clinical sessions on day 4. Peter Mazzone (Cleveland Clinic, USA) introduced the cancer session with a keynote presentation on "Breath analysis and cancer – where have gotten to and where are we going?" and reviewed the efforts on using breath analysis for cancer screening and early diagnostics. Promising biomarkers may be found among non-volatile metabolites and VOCs that are produced as part of cellular metabolism. The composition of those compounds may be altered for cancerous cells and may be detectable in blood, urine or breath using a number of methods. A number of studies have shown significant correlations between such makers (in form of altered patterns of breath VOCs) and cancer. However, one must be careful to avoid being deceived by random correlations.

Matthew McCurdy (Baylor College of Medicine, USA) presented results from a study exploring the utility of exhaled NO as a biomarker for radiation pneumonitis. The results indicated elevation of eNO is predictive of radiation pneumonitis in esophageal but not lung cancer patients. Promising results on applying a novel nano artificial olfactory system (NaNose ®) to the analysis of breath samples from lung cancer patients were presented by Maggie Hakim (Techicon, Israel). The data indicate that the sensor can be used to discriminate non-small cell lung cancer from small cell lung cancer. Patrick McCann (University of Oklahoma, USA) discussed in his presentation whether how the Warburg effect may be used for cancer detection. The Warburg effect (already described in 1927) is based on an altered pyruvate metabolism in aerobic glycolysis for cancer cells and results in increased production of lactate (which is usually associated with anaerobic metabolism in normal cells). First results seem to indicate that this effect may be detectable in breath and link known metabolic effects of cancer directly to biomarkers in breath. Also in this session, Paul Rhodes (Metabolomx, Mountain View, CA, USA) talked on advances in colorimetric sensors in lung cancer detection in breath which have previously shown to be capable of identifying the presence of lung cancer and potentially identifying subtypes (Mazzone et al, 2012, J. Thoracic Oncology). He presented impressive results from the next generation colorimetric sensors that have a much larger number of distinct indicators drastically improved sensitivity compared to previous generations. The cancer session was concluded by a presentation of Daya Upadhyay Stanford University, USA) describing the detection of elevated levels of pro-oncogenic microRNAs in exhaled breath condensate pointing to the possibility of tumor derived microRNAs as a novel diagnostic tool for lung cancer, complementary to the VOC breath markers explored by others.

The second clinical session of day 4 on "infections and metabolism" was introduced by the keynote presentation "Determining infection agent identity in the lung through breath analysis" by Jane Hill (University of Vermont, USA). She presented results from in vivo studies of breath biomarkers for infections with a range of respiratory pathogens that were obtained by analyzing the exhaled breath of infected mice. Interestingly, comparing the VOC signatures to signatures obtained from head space sampling of bacterial volatile biomarkers from in vitro samples (bacteria growing on cell cultures) it was shown that there are noticeable differences in those markers. Therefore, markers found in in-vitro measurements of bacterial infection may not be good predictors of markers to be useful for diagnosing infectious bacterial disease in vivo. Michael Schivo (University of California Davis, USA) presented results from an in vitro study of VOCs from uninfected and human rhinovirus infected bronchial epithelial cells showing different expression levels of VOCs for the two types of cells. Continuing the theme of in vitro profiling of VOCs produced by infected cells Alexander Aksenov (University of California Davis, USA) described the results from a SPME GC-MS study of VOCs from lymphoblastoid cells infected with various strains of influenza that showed the production of esters and oxygenated compounds attributed to increased oxidative stress during infection. Ana Guaman's (Institute for Bioengineering of Catalonia, Spain) presentation on detecting sepsis by breath analysis with ion mobility

spectrometry described promising results from a study that was based on an animal (rat) model that showed high specificity and sensitivity and suggest that exhaled breath analysis may be a very useful tool to diagnose and monitor sepsis. This second clinical session of day 4 concluded with a presentation by Juliane Obermeier (University of Rostock, Germany) on detection of volatile aldehydes and inflammation markers CO and NO using electrochemical sensors to analyze the breath of pigs and human patients with ppb sensitivity.

A session on day 5 covered volatiles and bowel disease. Norman Ratcliffe gave a fascinating keynote presentation on "Analyses of VOCs from Stool and Urine for Disease Diagnoses" that described investigating using VOCs detected from urine for the diagnosis of prostate cancer and bladder cancer as well as studying VOCs as markers for gastrointestinal diseases. Ross Butler (Adelaide, Australia) presented on using volatiles detected in exhaled breath from young children to assess their developing gut microbiome with results highlighting the dynamic nature of human microbiome enterotypes. Also in this session, Frederuk-Jan Van Schooten (Maastricht, Netherlands) presented promising results from a clinical study that analyzed breath VOCs from a number of patients with chronic inflammatory bowel disease by GC-MS in combination with chemometrics. A multivariate analysis was used to extract relevant information from the complex VOC profiles of patients and to demonstrate discrimination between active and remission form of Crohn's disease.

2.2 Breath Analysis for Environmental and Security Applications

On day 3 of the conference, one dedicated session of the conference covered environmental and security applications of breath analysis. The session started with a keynote presentation by Joachim Pleil (U.S. EPA, Research Triangle Park, USA on "exhaled breath aerosols – investigations of inflammatory proteins and opportunistic infections for environmental health," in which he described expanding the scope of breath analysis beyond VOCs to exhaled breath aerosols (EBA). EBA can easily be sampled by methods developed for environmental applications (e.g. PM2.5 filters). While EBA comprise only a small fraction of breath they may contain interesting markers for inflammation or infection (non-volatile, larger molecules, such as cytokines, or intact viruses or bacteria). A presentation on exploring potential national security applications of breath analysis was given by Matthias Frank (Livermore, USA) who described promising results from a study on detecting exposure to explosives or chemicals used in explosive manufacturing in exhaled breath of individuals. He also presented results from analyses of VOCs found in the headspace of cultures of biodefense related bacteria indicating that some of these bacteria emit characteristic VOCs during proliferation that may be useful in detecting the presence of such bacteria in the lung of exposed individuals. Also in this session, Ron Manginell (Sandia, Albuquerque, USA) described a handheld vapor analyzer for portable chemical and biological detection developed at Sandia National Laboratory that is based on MEMS-based analyzers with selective pre-concentration and GC detection stages. This sensor has been successfully applied to the detection of characteristic VOCs present at sub ppb levels in the headspace of growing bacteria.

2.3 Sampling Methods

The advantages and disadvantages of various breath sampling, collection and pre-concentration techniques occupied a significant proportion of the conference. The issue was introduced by Dr. Raed Dweik (Cleveland, USA), in a plenary session, entitled "Off-Line Testing for Volatiles- Strengths and Weaknesses". Offline testing allows transportation of breath to distant analysis devices, multiple breath samples to be collected and analyzed as one, potentially increasing sensitivity, and allows pre-concentration to be undertaken, again increasing sensitivity. There are however a number of drawbacks to off-line techniques. These include adsorption of the volatile onto the surface of the container, contamination of the breath sample from the container itself, either with volatiles used in the manufacture of the container, or, in containers used for multiple sample collection (as opposed to single use

containers), contamination due to inadequate cleaning. Off-line collection allows less flexibility in exploring the effects of pulmonary physiology and the breath maneuver on the concentration of breath volatile. This may be less important when the presence of a volatile in a sample is solely indicative of a disease state, as potentially might occur with volatiles produced by specific micro-organisms, but not by human metabolism, or when the difference in concentration of a volatile in disease states is much higher than in healthy states (for instance in end-stage renal failure). However, when differences between disease and normality are small, understanding the effects of the breath maneuver itself, and the impact of the collection equipment, becomes more important.

A number of speakers presented work exploring the utility of different pre-concentration techniques. Amy Scott-Thomas (Christchurch, New Zealand) presented data exploring different collection containers, different pre-concentration matrices, multiple breath maneuver, and the effects of transportation on potential volatile biomarkers of tuberculosis (REF, Scott Thomas). Yoshihiro Saito (Toyohashi, Japan) and Ditmar Hein (Mandala, Germany) presented data on needle-trap technology, incorporating adsorbent fiber and particles, contained within needles for easy pre-concentration and transport of volatile compounds.

The issues of collecting and analyzing breath samples from intubated and ventilated patients were addressed by a number of speakers, including Sharon Sturney (Christchurch, New Zealand), (REF, Sturney) who studied breath acetone in critically ill patients, while Michael Davis (Richmond, USA) presented data on exhaled breath condensate pH on ventilated patients on a Trauma Unit.

Finally, a spectacular scientific effort was presented by Laura Yeates (San Diego, USA) and Cristina Davis (Davis, USA) exploring off-line breath testing in marine mammals, especially the US Navy marine mammal program, and highlighted the extreme efforts and techniques undertaken by these and other researchers to collect breath samples from marine mammals, including dolphins and whales.

2.4 Novel Sensors and Instrumentation Advances

Several conference sessions covered advances in sensors and instrumentation for breath and trace gas analysis and are summarized here. (Advances in sampling techniques are described in the previous section.) Gary Hunter (NASA, Cleveland, USA) gave a fascinating keynote presentation on “Smart Sensor Systems for Human Health and Safety Applications” that described ongoing efforts to develop smart sensor systems for human health and safety applications including analyzing the composition of exhaled breath for monitoring the health status of an individual. Interestingly, the same core technologies can be used for a range of other trace gas detection problems including environmental monitoring and hazardous gas detection. Another overview of sensor technologies in use or under development for breath analysis was given by Tim Burch (Baldwin Park, USA). A larger number of presentations covered novel laser and spectroscopy approaches that could be useful for trace detection and breath analysis, including widely-tunable, narrow line width OPOs for mid-IR spectroscopy (Jean-Jacques Zondy, La Plaine Saint Denis, France), pure rotational spectrometry at microwave and millimeter wave frequencies that can detect a large number of low-molecular weight trace compounds simultaneously (Lawrence Hrubesh, Livermore, USA), a frequency comb laser instrument for multi analyte detection in breath (Konstantin Vodopyanov, Stanford, USA), a capillary absorption spectrometer for precision stable carbon isotope studies in small gaseous or ablated solid samples (Jim Kelly, Richland, USA), Laser Photoacoustic Spectroscopy to measure ethylene and ammonia as well as some other organic compounds in breath (Cristina Achim, Bucharest, Romania), a cavity ringdown spectroscopy based acetone breath analyzer (Chuji Wang, Mississippi State University, USA), cavity-enhanced, direct frequency comb spectroscopy for human breath analysis that could be used for massively parallel detection of multiple molecular compounds (Piotr Maslowski, Torun, Poland), infrared laser spectroscopy and its application to breath analysis using thermoelectrically cooled lasers emitting in the 3.3 um region to detect a number of

hydrocarbons of interest in breath (Joanne Shorter, Billerica, USA) and quantum cascade lasers for sensing applications (Pierre Bouzi, Princeton, USA). Other, non-spectroscopic sensor concepts that were described in presentations include portable Si:WO3 gas sensors for breath acetone monitoring (Marco Righettoni, Zurich, Switzerland), a compact high-speed nanosensor array based on carbon nanotubes (Ami Hannon, Moffet Field, USA), a mobile platform and telemetry for breath alcohol testing (Brad Keays, Cypress, USA), a personal mobile device for pulmonary lung function measurements that combines spirometry, peak expiratory flow and concentration measurements of select breath biomarkers (Alice Kwan, Moffet Field, USA), an electronic nose (the eNose) for exhaled breath analysis that is based on arrays of metal-oxide sensors (Jan Willem Gerritsen, Zutphen, Netherlands), a chemiresistor platinum nanowire array with expected high sensitivity due to the employed high resolution and high aspect ratio nanopatterns (Hae-Wook Yoo, Daejeon, South Korea),

Product commercialization and industry research were areas of focus on many of the days. In a keynote talk early in the conference, Michael Phillips presented perhaps the most established product, the BreathLink™ system for collecting and measuring specific metabolites from patients around the world (REF). He developed the BreathLink in 2006 to detect and diagnose Mycobacterium tuberculosis infections and his now moved this technology to the world health arena. This again represents a breakthrough development for human health, and one that should be further advertised. The company he founded, Menssana Research Inc., is focused on the translation of this technology to public health quickly. Research presented from the industry representatives more commonly derived from unique public-private partnerships. For example, Paul Rhodes from Metabolomx presented the recent successes of the colorimetric sensors, diverse chemically reactive indicator arrays that are capable of "fingerprinting" complex mixtures of volatiles, have been demonstrated to detect lung cancer in exhaled breath (REF Mazzone et al).

These talks in the scientific sessions were supplemented with focused talks from a number of industry representatives on two days. Brad Keays from SOBERLINK, Inc. devoted a talk to developing new technologies for qualitatively better monitoring of alcohol metabolites for patients in alcohol addiction and treatment programs. They have also worked to integrate existing proven technologies for seamless telemetry of testing results, better sobriety compliance and data management, allowing for seamless reporting and remote data storage. A talk by Jan Willem Garritesen from the eNose Company highlighted how their company has been developing electronic nose technology based on metal-oxide sensors. These devices are mass producible at low cost, and suitable for operating in harsh environments. All three companies are fostering academic scientist- private relationships with attendees at the conference to test the next generation of their products in clinical trials. These industry sessions also demonstrated less traditional approaches for development of breath analytical tools. Alice Kwan, a recent engineering graduate student at University of California, Davis working with Scanadu, Inc., a small bioengineering device company in San Francisco, CA, prototyped a portable inexpensive exhaled breath biomarker that she created while a student. It demonstrated the user-friendly, accurate, and portable external mobile device accessory that collects spirometry, PEF, exhaled nitric oxide (NO), carbon monoxide (CO), and oxygen (O2) concentration information from patients after two breath maneuvers. The device is designed to record and store the gathered test information and e-mails the results to a physician. Alice Kwan's talk detailed the advantages of both multidisciplinary teams and public-private partnerships.

2.5 Data Analysis Approaches

As complex data sets have emerged in breath analysis study trials, various sophisticated data analysis approaches have been reported in prior years. This trend continued as a theme in the Sonoma conference, and various researchers explained their approaches for statistical analysis of large data sets. While some researchers rely on traditional simple statistical tools, others employ methods such as pattern recognition and machine learning algorithms. In all cases, advantages and disadvantages were discussed. Most

notably, the possibility of establishing statistically robust correlations between a breath biomarker and a disease, simply due to the large number of independent variables in those systems (e.g. "voo-doo correlations"). Similarly, researchers urged caution when using machine learning techniques to look for patterns in data, as these approaches do not necessarily always identify biologically relevant compounds. In addition to numerical analysis methods, Joachim Pleil also introduced heat maps as a promising method of data visualization, especially for complex clinical trials.

In addition to researcher talks on their own topics, Pascal Girard from Oracle, Inc. gave a keynote presentation entitled "How to Deal with Big Data" which dealt with Oracle's new work with the National Cancer Institute. He focused on data attribution within complex systems, and how to annotate large data bases that contain heterogeneous pieces of information. While not directly applicable to the breath field at this time point, it seems possible that these types of approaches may help elucidate breath biomarkers across clinical trials in the future.

3. Open Discussions

Wolf Miekisch and Cristina Davis led a group session on the loosely-titled, but critical topic of "What are the open hard questions in our field?" The purpose was to highlight key knowledge gaps as well as foster some agreement on methodological and study design gaps in breath research. This session served to set the tone for the remainder of the conference. Not surprisingly, missed communication in interdisciplinary research efforts was a common theme in many of the comments. For example, while many novel platforms for analyte measurements were presented at the conference, there was frustration over the lack of recognized standards for analytes isolated from either exhaled gas or condensate, e.g. "isn't it time to agree upon a set of standard concentrations for gas and EBC that can be used to compare spectrometer platforms?" Frustrations in this area were repeatedly voiced and it was felt to be a major shortcoming in the field, and one that could potentially be addressed with published position papers. All participants recognized that consensus papers may be premature at this juncture, particularly given the numerous discovery studies that are ongoing with different breath collection protocols and assessment tools being used, but statements, however fluid, would still advance the field.

Other focused questions derived from this central concern. For example, "what devices should we agree upon for collection of exhaled gas and EBC?", or "how do we handle these samples, and at what temperature and for what time period? Similarly, "why aren't protein and metabolite levels normalized to total protein, sample volume, etc. in the same manner across studies?" It was readily acknowledged that these common issues all affect measurements and should be resolved. They continue to hamper research progress in this field. Finally, it was stated by some of the field leaders that all clinical and translational research efforts in this field must state their Institutional Review Board approvals, to bring this research to higher level. The Sonoma conference was deliberately designed to mix near-equal numbers of chemists, engineers, and physician scientists. In this regard, the program was a success as sessions varied greatly each day. Even with the frequent juxtaposition of talks on biomarker and spectrometer development, however, it was clear that it will take additional time and effort to bridge to some of the language and communication barriers that exist among the research fields. Some common problems can be solved within teams, but much of the technological and clinical research work remains too specialized for others to contribute easily.

"How do we promote the breath research field?" was another critical question posed. The modern breath research field remains in its infancy; it is a time of high risk research but with tremendous potential to improve human health. Discussion of how the interdisciplinary nature of the research makes it difficult to place in specific funding mechanisms and specific agencies was generally in agreement. While this was readily acknowledged by participants, there was no cohesive understanding of how the breath research field should pursue greater visibility jointly. Henry Couto, a journalist who runs the website Breathworld,

traveled from Brazil to attend the conference and proposed his internet-based platform as a way to more widely publicize the research in this field. However, while novel and potentially advantageous, this mechanism may not serve the interests of the collected researchers. Still, recent successes in lung cancer and asthma are two examples of breath research that would resonate with the public. Mechanisms to better communicate the importance of this field of research will be a challenge for years to come, and could impact funding from government agencies.

Ultimately, breath analysis technology could be instrumental in establishing a "personalized medicine" platform in the domain of medical diagnostics. A majority of attendees described, for example, how a sensor that could allow a clinician to determine whether a patient with new onset cough has a viral or bacterial bronchitis or an allergic flare of asthma would be highly advantageous. When such a device is easy to use, provides reliable and relevant information that can be acted upon, and can be incorporated into the daily work flow of a busy physician's office or and environmental researcher's protocol, the commercialization of such technology is obvious. Scientists and industry representatives alike repeatedly emphasized this issue, however, few had the wherewithal and experience to navigate the FDA IDE process alone. The amount of intellectual property that will be generated in this field in the next years will be massive. Who will ferry this property through the regulatory process and how is not clear. The private-public partnership ideal presented in a number of the talks admittedly fractures due to local competition, contract and funding issues.

Some prototype technologies may be exempt from the IDE regulations under regulation 21 CFR 812.2(c)), if the breath device is a "diagnostic device and if it is: noninvasive, does not require an invasive sampling procedure that presents significant risk, does not by design or intention introduce energy into a subject, and is not used as a diagnostic procedure without confirmation by another medically established diagnostic product or procedure. Many investigative devices will require a full IDE application submission, however, and many attendees expressed support needs in this area. The NIH has begun to recognize these needs in the U.S. and at least some institutions have support through the programs established in the Clinical and Translational Science Awards. Two of the authors work closely with the expert support in the UC Davis Clinical and Translational Science Center (CTSC) who have clinical research trials support unit to assist in submission with FDA applications. Many more such entities are needed to help further the breath analysis field.

4. Meeting Sponsorship

This is the third year that the University of California Davis Clinical and Translational Science Center (CTSC) and the Lawrence Livermore National Laboratory (LLNL) have partnered together to host the "*Breath Analysis for Biomedicine and National Security: Sensor Design Issues and Strategies for Biomarker Discovery"* meeting and this is the first year that the two organizations worked together to organize the 2012 International Meeting in Sonoma, CA. The success of the International meeting was attributed to the support from the host organizations, in particular the support that came from the Division of Pulmonary and Critical Care from UC Davis, as well as from five companies (MGC Diagnostics, Aerocrine, PAS Technology, Respiratory Research, and Shinwa Chemical Industries, Ltd.) and one University organization (The Center for Biophotonics Science and Technology at UC Davis). The tiered sponsorship levels ranged from Basic, where the organization's logo would be acknowledged on the meeting website and printed materials/meeting brochure, to Platinum, where an organization was additionally provided space to set-up an exhibit table during the Industry-sponsored receptions/poster sessions as well as a timeslot on the agenda during one of the Industry Sessions where the organization was able to make an introduction to the meeting attendees. As mentioned, the above stated sponsoring and affiliate groups graciously helped with many aspects and the meeting is very grateful to these organizations for their sponsorship. Additional information on the sponsoring companies can be found on the meeting website, http://breathanalysis.ucdavis.edu/sponsors.html.

Michael Phillips and Mike Schivo moderated the first Industry and Product Development Demonstration Session on the evening of day 2 of the meeting. Pascal Girard from Oracle, Inc. kicked off this session with a Keynote Address entitled, "How to Deal with Big Data: Oracle's new work with the National Cancer Institute and how it could help the breath analysis community". Two additional industry presentations followed Pascal's keynote. Rafi Baddour from Respiratory Research, Inc. presented on the topic of "Breath Collection at the Home, Job Site, Clinic, and ICU" and Zvi Yaniv from Applied Nanotech, Inc. presented on the topic of "EZKnowz – From Life Science Applications to Healthcare".

Matthias Frank moderated the final Industry and Product Development Demonstration Session on the evening of day 4 of the meeting in which three industry representatives presented. Brad Keays from SOBERLINK, Inc. presented on the topic of "Mobile Platforms and Telemetry for Breath Sobriety Testing", Alice Kwan from Scanadu, Inc. presented on the topic of "Personal Mobile Devices for Pulmonary Lung Function Measurements", and Jan Willem Gerritsen from The eNose Company presented on the topic of "Mass Applicable Electronic Nose for Exhaled-Breath Analysis".

Following each Industry Session on day 2 and 4, an Industry-sponsored Reception and Poster Session/Technology Showcase was held for the attendees. Nearly 100+ attendees had the opportunity to view 28 scientific posters presented by graduate students, postdoctoral researchers, physicians, government, and industry representatives. The industry sponsors were also available for hands on demonstrations of their technology at their respective exhibit tables. The mingling between the poster session and the industry exhibit tables provided ample opportunity for networking, discussion of on-going research collaborations, exploration of potential future collaborations, and consideration of teaming for competitive grant proposal submissions to federal funding agencies. The interactions with the industry participants also allowed for discussion on the near-term research trends that may have the potential to yield first generations of breath analysis sensor platforms.

5. Closing Thoughts

While the field of breath analysis has continued to mature at a rapid pace in the last half-decade, much further work is still needed to translate this research into meaningful clinical tests for the public. Public-private partnerships will almost certainly be needed to move many research projects out into viable commercial technologies, and this will likely require multidisciplinary teams for final product development. It seems likely that more standardization in sampling and detection strategies will evolve over time, although that may grow at a pace dictated by the research community. Finally, as breath biomarker discovery is validated, it will be necessary to test these predictive markers in larger patient cohorts. This will likely require commitment again from public-private partnerships to fund and logistically organize the clinical validation trials for needed for regulatory approval.

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